Refine Search

Search Results -

Terms	Documents
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Search: L1

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DATE: Wednesday, April 20, 2005 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
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L1	liposome adj10 disulfide	68	L1

END OF SEARCH HISTORY

First Hit Fwd Refs Previous Doc Next Doc Go to Doc#

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L1: Entry 4 of 68 File: USPT Dec 9, 2003

DOCUMENT-IDENTIFIER: US 6660525 B2
TITLE: Therapeutic liposome composition and method

Detailed Description Text (34):
In studies performed in support of the present invention, described below, liposomes having a releasable surface coating of polyethylene glycol were prepared, where the polyethylene glycol chains were attached to the liposome by a labile, disulfide bond. The liposomes were administered to mice and allowed to distribute. A reducing agent was administered to effect release of the polymer chains. Tissue analysis of the mice lung and liver indicated that the hydrophilic polymer coating was released, as evidenced by retention of the liposomes in these organs.

Detailed Description Text (105):
In studies performed in support of the invention, liposomes having a releasable coating of PEG were prepared and administered to mice, as described in Example 1. The releasable coating of PEG was formed by including in the liposomes PEG attached to DSPE through a thiolytically cleavable disulfide linkage (PEG-DTP-DSPE), prepared according to the scheme shown in FIG. 5.

Previous Doc Next Doc Go to Doc#

First Hit Fwd Refs Previous Doc Next Doc Go to Doc#

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L1: Entry 6 of 68 File: USPT Jul 1, 2003

DOCUMENT-IDENTIFIER: US 6586002 B2
TITLE: Enhanced circulation effector composition and method

Detailed Description Text (43):
2. Coupling by 3-(2-pyridyldithio) propionamide. The reaction of dithio propionamides with the sulfhydryl group produces coupling to the sulfhydryl-containing molecules via a disulfide linkage. Disulfide exchange occurs readily at pH 8, in a nonreducing environment. The method involves reaction of a thiol group in a peptide with a liposome prepared to contain PE-PEG (2-pyridyldithio) propionamide). The reaction couples the protein to the liposomes through a disulfide linkage as illustrated in FIG. 10 (compound XXXIV).

Previous Doc Next Doc Go to Doc#

First Hit Fwd Refs Previous Doc Next Doc Go to Doc#
Generate Collection Print

L1: Entry 18 of 68 File: USPT Jan 2, 2001

DOCUMENT-IDENTIFIER: US 6169078 B1
TITLE: Materials and methods for the intracellular delivery of substances

Brief Summary Text (12):
A further aspect of the subject invention pertains to convenient methods of synthesis for disulfide-containing cationic lipids. In a specific embodiment, the lipid, 1,2-dioleoyl-sn-glycero-3-succinyl-2-hydroxyethyl disulfide ornithine conjugate (DOGSDSO), can be synthesized and used to prepare liposomes in combination with L-dioleoyl phosphatidylethanolamine (DOPE). The disulfide bond of DOGSDSO is cleaved by reductive media leading to destabilization of the liposome/DNA complex, thus increasing the release of DNA compared to a non-disulfide-containing analog.

Previous Doc Next Doc Go to Doc#

L1: Entry 20 of 68 File: USPT Nov 28, 2000

DOCUMENT-IDENTIFIER: US 6153434 A
TITLE: Methods for the intracellular delivery of substances

Brief Summary Text (14):
A further aspect of the subject invention pertains to convenient methods of synthesis for disulfide-containing cationic lipids. In a specific embodiment, the lipid 1,2-dioleoyl-sn-glycero-3-succinyl-2-hydroxyethyl disulfide ornithine conjugate (DOGSDSO), can be synthesized and used to prepare liposomes in combination with L-dioleoyl phosphatidylethanolamine (DOPE). The disulfide bond of DOGSDSO is cleaved by reductive media leading to destabilization of the liposome/DNA complex, thus increasing the release of DNA compared to a non-disulfide-containing analog. In another embodiment, the lipid Cholesteryl hemidithiodiglycolyl tris(aminoethyl)amine (CHDTAEA) can be synthesized and used to prepare liposomes according to the present invention.

Detailed Description Text (33):
The results of transgene expression demonstrated that CHDTAEA liposomes had greater transfection activity than its non-disulfide analog CHSTAEA in both CHO and SKnSH cells.

Detailed Description Text (88):
DNA was complexed with a disulfide cationic liposome CHDTAEA/DOPE or its non-disulfide cationic liposome analog CHSTAEA/DOPE at the cationic lipid to DNA ratio of 2/1. As indicated in FIG. 4, DNA was tightly complexed by both cationic liposomes. In the absence of glutathione, disulfide liposomes/DNA complexes did not release DNA after 20-hour incubation in PBS at 37.degree. C. In the presence of 10 mM of glutathione, >50% of DNA was released from complexes after the incubation. In both reductive and non-reductive environments, non-disulfide liposome CHSTAEA/DNA complexes did not release any DNA. The results suggested cationic liposome/DNA complexes were stable, and that cellular reductive substances (i.e., glutathione) can destabilize the complexes and help DNA to dissociate from liposomes. The complexes with the ratios of cationic liposome/DNA from 3/1 to 5/1 were also tested in the release assay with similar same results.